

APPENDIX C. A SCIENTIFIC ABSTRACT

Unresectable and metastatic bladder cancer responds to combination chemotherapy although most patients ultimately die of the disease; long term survival is achieved mainly through cystectomy in patients with organ-confined disease. An objective of ongoing clinical research is to optimize the use of chemotherapy, surgery, and novel therapeutic modalities in treatment of patients with locally advanced disease. The tumor suppressor gene p53 is frequently mutated in bladder cancer and its loss is associated with rapid progression and shorter survival. This proposal encompasses efforts to further the development of p53 gene therapy for bladder cancer in a Phase I clinical trial of the replication defective adenoviral vector Ad-p53, administered by intravesical instillation in patients with locally advanced and metastatic bladder cancer. We will define the maximum tolerable dose and toxicity of intravesically administered Ad-p53. This is a novel route of administration for an adenoviral vector in humans and this would be the first clinical demonstration that infection with an adenoviral vector and expression of a transferred gene is possible using this method. Bladder cancer is ideally suited for this purpose because it is accessible by cystoscopy for direct examination and biopsy. Cystectomies are not planned for patients in the study following gene therapy so that we will have an opportunity to study the *in vivo* effects over a one year period.